NMCP COVID-19 Literature Report #53: Wednesday, 30 December 2020

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Purpose: These weekly reports, published on Fridays, are curated collections of current research, evidence reviews, special reports, grey literature, and news regarding the COVID-19 pandemic that may be of interest to medical providers and leadership. All reports are available online at https://nmcp.libguides.com/covidreport. Access is private; you will need to use the direct link or bookmark the URL, along with the case-sensitive password "NMCPfinest".

Disclaimer: I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, things are changing rapidly, with new research and potentially conflicting literature published daily. Please feel free to reach out with questions, suggestions for future topics, or any other feedback.

Statistics

Global today: 82,100,010 confirmed cases and 1,793,150 deaths in 191 countries/regions

18 DEC 2020: 75,179,482 confirmed cases and 1,667,124 deaths in 191 countries/regions

11 DEC 2020: 69,765,806 confirmed cases and 1,585,221 deaths in 191 countries/regions

*United States** top 5 states by cases (Virginia is ranked 20th)

	TOTAL US	CA	TX	FL	NY	IL
Cases	19,516,147	2,232,911	1,730,391	1,292,252	950,473	948,006
Tests	245,005,299	32,374,471	13,591,767	15,443,777	24,913,524	13,591,767
Deaths	338,656	24,988	27,282	21,409	37,687	17,596

*see census.gov for current US Population data; NA: not all data available JHU CSSE as of 1000 EDT 30 December 2020

Virginia	Total (state)	Chesapeake	Hampton	Newport News	Norfolk	Portsmouth	Suffolk	Virginia Beach
Cases	344,345	9,224	4,236	5,892	8,697	4,421	3,914	16,294
Hospitalizations	17,910	611	195	205	554	429	229	736
Deaths	4,984	99	48	69	105	78	90	147

VA DOH as of 1000 EDT 30 December 2020

2020: A Pandemic Timeline

Taken from the Johns Hopkins Center for Health Security Situation Reports newsletters:

- *"COVID-19 at Six Months" (02 July 2020)*
- *"A Year with COVID-19" (29 December 2020)*

December 31 : Wuhan Municipal Health Commission publishes the initial report of unidentified pneumonia, potentially linked to a local market

January 6 : US CDC issues a Level 1 travel watch for Wuhan, China

January 11 : First reported COVID-19 death in China

January 13 : First COVID-19 case reported outside of China

January 21 : First COVID-19 case reported in the US

January 23 : China implements "lockdown" in Wuhan

January 24 : First imported COVID-19 cases reported in Europe (France)

January 27 : US CDC issues Level 3 travel warning for China, recommending against non-essential travel

January 27 : First documented SARS-CoV-2 transmission in Europe (Germany)

January 29 : First COVID-19 cases reported in Eastern Mediterranean Region (United Arab Emirates)

January 30 : WHO declares COVID-19 a Public Health Emergency of International Concern

January 30 : US CDC confirms first domestic transmission of SARS-CoV-2

January 31 : US implements travel restrictions for Mainland China

February 5 : The Diamond Princess cruise ship is quarantined in Yokohama, Japan, due to an ongoing COVID-19 outbreak onboard that resulted in at least 712 confirmed cases, including 9 deaths

February 25 : First COVID-19 case reported in the African Region (Algeria)*

February 27 : South Korea surpasses China as #1 globally in terms of daily COVID-19 incidence

February 29 : US implements travel restrictions for Iran

March 4 : Seattle and King County, Washington (US), advises high-risk individuals to avoid large gatherings

March 8 : Italy implements "lockdown" for affected areas of the Lombardy region in Northern Italy

March 10 : Italy expands "lockdown" measures to the entire country

March 11 : US implements travel restrictions for all of Europe

March 11 : WHO declares COVID-19 a pandemic

March 13 : US declares the COVID-19 epidemic to be a national emergency

March 14 : US implements travel restrictions for the UK and Ireland

March 15 : National "lockdown" goes into effect in Spain

March 16 : Six counties in the San Francisco Bay Area, California (US), issue the country's first shelter-in-place orders

March 18 : The WHO announces the SOLIDARITY Trial, a global collaboration to conduct clinical trials for prospective COVID-19 medical countermeasures

March 19 : California (US) issues the first statewide "stay at home" order

March 23 : The University of Oxford (UK) begins enrolling patients for the RECOVERY Trial, a nationwide clinical trial effort in the UK for COVID-19 MCMs

March 24 : National "lockdown" ordered in India

March 24 : The International Olympic Committee announces that the 2020 Olympic Games, scheduled to be hosted in Japan, are postponed

March 27 : US CDC expands travel restrictions to cover *all* other countries

March 28 : US CDC issues domestic travel advisory for New York, New Jersey, and Connecticut

March 28 : Italy surpasses China as #1 globally in terms of cumulative COVID-19 incidence

March 29 : US surpasses Italy as #1 globally in terms of cumulative COVID-19 incidence (and remains #1 today)

[edited to add March 31: the first NMCP COVID-19 Literature Report]

April 4 : 1 million global cases

May 15 : US government unveils Operation Warp Speed, a program to drive development and production of medical countermeasures against COVID-19

May 17 : WHO reports more than 100,000 new cases in a single day

May 23 : 5 million global cases

May 24 : US implements travel restrictions for Brazil

May 28 : US surpasses 100,000 cumulative reported COVID-19 deaths

May 29 : New York (US) enters Phase 1 of recovery (NYC on June 8)

June 8 : New Zealand declares SARS-CoV-2 eliminated

June 11 : European Commission recommends that European countries remove internal border restrictions by June 15 to enable travel within the continent

June 29 : 10 million global cases

June 30 : 500,000 global deaths

June 30 : European Council announces that European countries would lift travel restrictions for 15 countries beginning July 1

July 7: Brazilian President Jair Bolsonaro tests positive for SARS-CoV-2

July 17: India surpasses 1 million cumulative cases

July 20: The WHO reports 600,000 cumulative deaths globally

July 22: China initiates vaccination of essential workers under an emergency authorization

July 23: The WHO reports 15 million cumulative cases globally

July 24: The US summer surge peaks at 67,187 new cases per day

July 28: The US surpasses Brazil as #1 globally in terms of daily mortality

July 29: The US surpasses 150,000 cumulative deaths

August 6: India surpasses the US as #1 globally in terms of daily incidence

August 7: 700,000 global deaths

August 9: The US surpasses 5 million cumulative cases

August 9: New Zealand reports 100 consecutive days without a documented case of domestic transmission

August 10: Brazil surpasses 100,000 cumulative deaths

August 12: 20 million global cases

August 15: South America's first surge peaks at 75,932 new cases per day

August 22: Brazil surpasses the US to regain #1 globally in terms of daily mortality

August 23: 800,000 global deaths

August 26: India surpasses Brazil as #1 globally in terms of daily mortality

September 1: Russia surpasses 1 million cumulative cases

September 10: 900,000 global deaths

September 16: India surpasses 5 million cases

September 18: 30 million global cases

September 22: The US surpasses 200,000 deaths

September 29: 1 million global deaths

October 1: US President Donald Trump tests positive for SARS-CoV-2

October 3: India surpasses 100,000 cumulative deaths

October 4: The Great Barrington Declaration is published, calling for policies to achieve "herd immunity" through natural infection

October 9: Brazil surpasses 5 million cases

October 19: 40 million global cases

October 19: Spain surpasses 1 million cumulative cases

October 20: The US surpasses India to regain #1 globally in terms of daily incidence

October 21: Argentina surpasses 1 million cumulative cases

October 21: the US surpasses India to regain #1 globally in terms of daily mortality

October 24: France surpasses 1 million cumulative cases

October 26: Colombia surpasses 1 million cumulative cases

October 29: The WHO reports more than 500,000 new cases in a single day for the first time

October 30: The US becomes the first country to report more than 100,000 new cases in a single day

November 1: The United Kingdom surpasses 1 million cumulative cases

November 8: 1.25 million global deaths

November 8: Europe's "second wave" peaks at 287,101 new cases per day

November 9: 50 million global cases

November 9: The US surpasses 10 million cases

November 12: Italy surpasses 1 million cumulative cases

November 16: Mexico surpasses 1 million cumulative cases

November 17: The US FDA issues an Emergency Use Authorization (EUA) for the first fully at-home SARS-CoV-2 test kit

November 18: Pfizer announces the completion of the Phase 3 clinical trials for its SARS-CoV-2 vaccine, developed in collaboration with BioNTech

November 21: Mexico surpasses 100,000 cumulative deaths

November 26: 60 million global cases

November 27: Germany surpasses 1 million cumulative cases

November 30: Moderna announces the completion of the Phase 3 clinical trials for its SARS-CoV-2 vaccine

December 2: The UK issues emergency authorization for the Pfizer/BioNTech vaccine

December 3: Poland surpasses 1 million cumulative cases

December 3: The US becomes the first country to report more than 200,000 new cases in a single day

December 4: Iran surpasses 1 million cumulative cases

December 4: 1.50 million global deaths

December 5: Russia opens vaccination to the public, using its Sputnik V vaccine

December 8: The US surpasses 15 million cases

December 8: The UK administers its first vaccinations to the public, using the Pfizer/BioNTech vaccine

December 10: Turkey surpasses 1 million cumulative cases

December 11: US FDA issues an EUA for the Pfizer/BioNTech SARS-CoV-2 vaccine

December 13: 70 million global cases

December 14: The US surpasses 300,000 deaths

December 14: The US administers its first vaccinations to the public, using the Pfizer/BioNTech vaccine

December 15: The US FDA issues an EUA for the first fully at-home SARS-CoV-2 diagnostic test available without a prescription

December 17: French President Emmanuel Macron tests positive for SARS-CoV-2

December 18: US FDA issues an EUA for the Moderna SARS-CoV-2 vaccine

December 19: India surpasses 10 million cases

December 21: The first COVID-19 cases are reported in Antarctica, the last of the 7 continents to report a case

December 23: The US reports 1 million vaccine doses administered

December 24: Peru surpasses 1 million cumulative cases

December 24: Ukraine surpasses 1 million cumulative cases

December 26: European countries administer the first vaccinations to the public, using the Pfizer/BioNTech vaccine

December 27: 1.75 million global deaths

December 29: The UK begins administering the second doses of the Pfizer/BioNTech vaccine

Special Reports

Mott: [C.S. Mott Children's Hospital National Poll on Children's Health 2020 survey]

"The of child health concerns asked a national sample of parents to rate the top health concerns for US children and teens aged 0-18 years. The 2020 top child health concerns are:

- Overuse of social media/screen time (72%)
- Bullying/cyberbullying (62%)
- Internet safety (62%)
- Unhealthy eating (59%)
- Depression/suicide (54%)
- Lack of physical activity (54%)
- Stress/anxiety (54%)
- Smoking/vaping (52%)
- Drinking or using drugs (50%)

When the 2020 Top 10 results are examined separately by the racial/ethnic groups of the parents, some key differences and similarities among the groups stand out….

Other notable differences by racial /ethnic group include Black parents as the only group that rates gun injuries and unequal access to health care as a Top 10 concern and White parents as the only group to rate lack of physical activity in the Top 10."

2020 Top 10 Child Health Concerns

Among Black Parents		Among Hispanic Parents		Among White Parents	
1 Racism	82%	1 Overuse of social media	73%	1 Overuse of social media	72%
2 COVID	73%	2 Bullying/cyberbullying	72%	2 Bullying/cyberbullying	58%
3 Overuse of social media	70%	3 Internet safety	72%	3 Internet safety	57%
4 Unhealthy eating	68%	4 Smoking/vaping	67%	4 Unhealthy eating	56%
5 Internet safety	67%	5 Drinking or using drugs	67%	5 Lack of physical activity	53%
6 Bullying/cyberbullying	66%	6 Racism	65%	6 Stress/anxiety	51%
7 Poverty	66%	7 Depression/suicide	64%	7 Depression/suicide	49%
8 Drinking or using drugs	62%	8 COVID	64%	8 Smoking/vaping	46%
9 Unequal healthcare access	62%	9 Stress/anxiety	62%	9 Child abuse & neglect	42%
10 Gun injuries	61%	10 Child abuse & neglect	61%	10 Drinking or using drugs	41%

Source: C.S. Mott Children's Hospital National Poll on Children's Health, 2020

Selected Literature: Peer-Reviewed Journals

Date given is the date published or posted online; often these papers are ahead of print.

29 December 2020

JAMA: National Trends in the US Public's Likelihood of Getting a COVID-19 Vaccine—April 1 to December 8, 2020

> "This internet survey study describes trends in respondents saying they were likely to accept vaccination for COVID-19 overall and by age, sex, race, and education between April and December 2020."

JAMA Cardiol: Assessment of Neutrophil Extracellular Traps in Coronary Thrombus of a Case Series of Patients With COVID-19 and Myocardial Infarction

> "Question: What is the role of neutrophil extracellular traps in coronary thrombosis in patients with coronavirus disease 2019 (COVID-19) and myocardial infarction?
>
> Findings: This case series report demonstrated a high burden of neutrophil extracellular traps (median density, 61%) in the coronary thrombi of 5 patients with ST-elevated myocardial infarction and COVID-19, compared with a historical series of 50 patients without COVID-19 (median NET density, 19%), which was a significant difference.
>
> Meaning: Targeting intravascular neutrophil extracellular traps might be a relevant goal of treatment and a feasible way to prevent coronary thrombosis in patients with severe COVID-19."

JAMA Netw Open: Patient Characteristics Associated With Telemedicine Access for Primary and Specialty Ambulatory Care During the COVID-19 Pandemic

> "Question: What sociodemographic factors are associated with higher use of telemedicine and the use of video (vs telephone) for telemedicine visits for ambulatory care during the coronavirus disease 2019 (COVID-19) pandemic?
>
> Findings: In this cohort study of 148 402 patients scheduled for primary care and medical specialty ambulatory telemedicine visits at a large academic health system during the early phase of the COVID-19 pandemic, older age, Asian race, non-English language as the patient's preferred language, and Medicaid were independently associated with fewer completed telemedicine visits. Older age, female sex, Black race, Latinx ethnicity, and lower household income were associated with lower use of video for telemedicine care.
>
> Meaning: This study identified racial/ethnic, sex, age, language, and socioeconomic differences in accessing telemedicine for primary care and specialty ambulatory care; if not

addressed, these differences may compound existing inequities in care among vulnerable populations."

23 December 2020

Lancet Diabetes Endocrinol: Risks of and risk factors for COVID-19 disease in people with diabetes: a cohort study of the total population of Scotland

"In this cohort study, we captured the data encompassing the first wave of the pandemic in Scotland, ie, from March 1, 2020, when the first case was identified, to July 31, 2020, when infection rates had dropped sufficiently that shielding measures were officially terminated. Including critical care-treated and out-of-hospital deaths from COVID-19 for the first time, as well as hospitalised deaths, we showed that the risk of fatal or critical care unit-treated COVID-19 is increased by 2·4 times in type 1 diabetes and 1·4 times in type 2 diabetes. For the first time, to our knowledge, we have shown that people with recent admissions history for hypoglycaemia and diabetic ketoacidosis have an increased risk of severe or fatal disease. People with a history of smoking had increased risks. Prior specific comorbidities, including heart disease, liver disease, and chronic lower respiratory disease, also increased risk. We showed for the first time, to our knowledge, that being exposed to more drug classes and having more previous hospital admissions are markers of risk. A risk prediction model achieved a C-statistic of 0·85. We provided a Shiny app to give the reader a sense of how individual risk factor profiles in people with diabetes translate into elevated risks compared with those without diabetes.

During phases of the COVID-19 pandemic, when the effective reproduction number is high, those people with diabetes who are most at risk might warrant special protection measures. A risk prediction score based on medical history can usefully identify those with diabetes who are most at risk, and we provide an example of such a score."

NEJM: Antibody Status and Incidence of SARS-CoV-2 Infection in Health Care Workers

"We investigated the incidence of SARS-CoV-2 infection confirmed by polymerase chain reaction (PCR) in seropositive and seronegative health care workers attending testing of asymptomatic and symptomatic staff at Oxford University Hospitals in the United Kingdom. Baseline antibody status was determined by anti-spike (primary analysis) and anti-nucleocapsid IgG assays, and staff members were followed for up to 31 weeks. We estimated the relative incidence of PCR-positive test results and new symptomatic infection according to antibody status, adjusting for age, participant-reported gender, and changes in incidence over time.

A total of 12,541 health care workers participated and had anti-spike IgG measured; 11,364 were followed up after negative antibody results and 1265 after positive results, including

88 in whom seroconversion occurred during follow-up. A total of 223 anti-spike–seronegative health care workers had a positive PCR test (1.09 per 10,000 days at risk), 100 during screening while they were asymptomatic and 123 while symptomatic, whereas 2 anti-spike–seropositive health care workers had a positive PCR test (0.13 per 10,000 days at risk), and both workers were asymptomatic when tested (adjusted incidence rate ratio, 0.11; 95% confidence interval, 0.03 to 0.44; P=0.002). There were no symptomatic infections in workers with anti-spike antibodies. Rate ratios were similar when the anti-nucleocapsid IgG assay was used alone or in combination with the anti-spike IgG assay to determine baseline status.

The presence of anti-spike or anti-nucleocapsid IgG antibodies was associated with a substantially reduced risk of SARS-CoV-2 reinfection in the ensuing 6 months."

Sci Immunol: Discordant neutralizing antibody and T cell responses in asymptomatic and mild SARS-CoV-2 infection

"Understanding the nature of immunity following mild/asymptomatic infection with SARS-CoV-2 is crucial to controlling the pandemic. We analyzed T cell and neutralizing antibody responses in 136 healthcare workers (HCW) 16-18 weeks after United Kingdom lockdown, 76 of whom had mild/asymptomatic SARS-CoV-2 infection captured by serial sampling. Neutralizing antibodies (nAb) were present in 89% of previously infected HCW. T cell responses tended to be lower following asymptomatic infection than in those reporting case-definition symptoms of COVID-19, while nAb titers were maintained irrespective of symptoms. T cell and antibody responses were sometimes discordant. Eleven percent lacked nAb and had undetectable T cell responses to spike protein but had T cells reactive with other SARS-CoV-2 antigens. Our findings suggest that the majority of individuals with mild or asymptomatic SARS-CoV-2 infection carry nAb complemented by multispecific T cell responses at 16-18 weeks after mild or asymptomatic SARS-CoV-2 infection."

22 December 2020

EClinicalMedicine: COVID-19 risk, disparities and outcomes in patients with chronic liver disease in the United States

"People who have serious underlying medical conditions, including chronic liver disease (CLD), might be at higher risk for severe illness from COVID-19. Evidence showed that SARS-CoV-2 virus damages the liver in infected patients and that pre-existing liver disease was associated with increased mortality in patients with COVID-19. However, it remains unknown whether patients with CLD are at increased risk for getting COVID-19 compared with individuals without CLD and how the risk for COVID-19 is further affected by age, gender and race.

This analysis of patient electronic health records (EHRs) quantifies for the first time the risks, racial disparities, and outcomes for COVID-19 in individuals with a CLD, including alcoholic cirrhosis, non-alcoholic cirrhosis, alcoholic liver damage, chronic hepatitis B, chronic hepatitis C, and chronic non-alcoholic liver disease.

Based on this analysis, patients with a CLD, especially African Americans with CLD, were at increased risk for both COVID-19 and its adverse outcomes, highlighting the need to protect these patients from exposure to virus infection."

Emerg Infect Dis: Antibody Responses 8 Months after Asymptomatic or Mild SARS-CoV-2 Infection

"Waning humoral immunity in coronavirus disease patients has raised concern over usefulness of serologic testing. We investigated antibody responses of 58 persons 8 months after asymptomatic or mildly symptomatic infection with severe acute respiratory syndrome coronavirus 2. For 3 of 4 immunoassays used, seropositivity rates were high (69.0%–91.4%)."

JAMA Intern Med: Variation in US Hospital Mortality Rates for Patients Admitted With COVID-19 During the First 6 Months of the Pandemic

"Question: Are hospital outcomes for patients with coronavirus disease 2019 (COVID-19) improving?

Findings: In this cohort study of 38 517 adults who were admitted with COVID-19 to 955 US hospitals, rates of 30-day mortality or referral to hospice varied from 9.06% to 15.65% in the best- and worst-performing quintiles. In the early months of the pandemic, 94% of hospitals in a subset of 398 improved by at least 25%, and the strongest determinant of improvements in hospital-level outcome was a decline in community rates of infection.

Meaning: All else being equal, COVID-19 mortality in hospitals seems to be lower when the prevalence of COVID-19 in their surrounding communities is lower."

JAMA Netw Open: Assessment of Air Contamination by SARS-CoV-2 in Hospital Settings

"Question: What is the level of air contamination from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in different hospital areas, and what factors are associated with contamination?

Findings: In this systematic review of 24 studies, 17% of air sampled from close patient environments was positive for SARS-CoV-2 RNA, with viability of the virus found in 9% of cultures.

Meaning: In this study, air both close to and distant from patients with coronavirus disease 2019 was frequently contaminated with SARS-CoV-2 RNA; however, few of these samples contained viable viruses."

JAMA Netw Open: Assessment of Maternal and Neonatal SARS-CoV-2 Viral Load, Transplacental Antibody Transfer, and Placental Pathology in Pregnancies During the COVID-19 Pandemic

"Question: What key biological characteristics of maternal severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and placental function and pathology have implications for vertical transmission and neonatal protection?

Findings: In this prospective cohort study including 127 pregnancies, there was no maternal viremia, placental infection, or vertical transmission of SARS-CoV-2. Compromised transplacental transfer of anti–SARS-CoV-2 antibodies with robust transfer of influenza-specific immunity and nonoverlapping placental expression of SARS-CoV-2 receptors angiotensin-converting enzyme 2 and transmembrane serine protease 2 were noted.

Meaning: These findings suggest that, although low rates of maternal viremia and patterns of placental SARS-CoV-2 receptor distribution may underlie the rarity of vertical transmission, reduced transplacental transfer of anti–SARS-CoV-2 antibodies may leave neonates at risk for infection."

MMWR: The Advisory Committee on Immunization Practices' Updated Interim Recommendation for Allocation of COVID-19 Vaccine — United States, December 2020

"On December 1, the Advisory Committee on Immunization Practices (ACIP) recommended that health care personnel and long-term care facility residents be offered COVID-19 vaccination first (Phase 1a).

On December 20, ACIP updated interim vaccine allocation recommendations. In Phase 1b, COVID-19 vaccine should be offered to persons aged ≥75 years and non–health care frontline essential workers, and in Phase 1c, to persons aged 65–74 years, persons aged 16–64 years with high-risk medical conditions, and essential workers not included in Phase 1b.

Federal, state, and local jurisdictions should use this guidance for COVID-19 vaccination program planning and implementation."

NEJM: A Neutralizing Monoclonal Antibody for Hospitalized Patients with Covid-19

"In this platform trial of therapeutic agents, we randomly assigned hospitalized patients who had Covid-19 without end-organ failure in a 1:1 ratio to receive either LY-CoV555 or matching placebo. In addition, all the patients received high-quality supportive care as background therapy, including the antiviral drug remdesivir and, when indicated, supplemental oxygen and glucocorticoids. LY-CoV555 (at a dose of 7000 mg) or placebo was administered as a single intravenous infusion over a 1-hour period. The primary outcome

was a sustained recovery during a 90-day period, as assessed in a time-to-event analysis. An interim futility assessment was performed on the basis of a seven-category ordinal scale for pulmonary function on day 5.

On October 26, 2020, the data and safety monitoring board recommended stopping enrollment for futility after 314 patients (163 in the LY-CoV555 group and 151 in the placebo group) had undergone randomization and infusion. The median interval since the onset of symptoms was 7 days (interquartile range, 5 to 9). At day 5, a total of 81 patients (50%) in the LY-CoV555 group and 81 (54%) in the placebo group were in one of the two most favorable categories of the pulmonary outcome. Across the seven categories, the odds ratio of being in a more favorable category in the LY-CoV555 group than in the placebo group was 0.85 (95% confidence interval [CI], 0.56 to 1.29; P=0.45). The percentage of patients with the primary safety outcome (a composite of death, serious adverse events, or clinical grade 3 or 4 adverse events through day 5) was similar in the LY-CoV555 group and the placebo group (19% and 14%, respectively; odds ratio, 1.56; 95% CI, 0.78 to 3.10; P=0.20). The rate ratio for a sustained recovery was 1.06 (95% CI, 0.77 to 1.47).

Monoclonal antibody LY-CoV555, when coadministered with remdesivir, did not demonstrate efficacy among hospitalized patients who had Covid-19 without end-organ failure."

Sci Immunol: Rapid generation of durable B cell memory to SARS-CoV-2 spike and nucleocapsid proteins in COVID-19 and convalescence

"Lasting immunity following SARS-CoV-2 infection is questioned because serum antibodies decline in convalescence. However, functional immunity is mediated by long-lived memory T and B (Bmem) cells. Therefore, we generated fluorescently-labeled tetramers of the spike receptor binding domain (RBD) and nucleocapsid protein (NCP) to determine the longevity and immunophenotype of SARS-CoV-2-specific Bmem cells in COVID-19 patients. A total of 36 blood samples were obtained from 25 COVID-19 patients between 4 and 242 days post-symptom onset including 11 paired samples. While serum IgG to RBD and NCP was identified in all patients, antibody levels began declining at 20 days post-symptom onset. RBD- and NCP-specific Bmem cells predominantly expressed IgM+ or IgG1+ and continued to rise until 150 days. RBD-specific IgG+ Bmem were predominantly CD27+, and numbers significantly correlated with circulating follicular helper T cell numbers. Thus, the SARS-CoV-2 antibody response contracts in convalescence with persistence of RBD- and NCP-specific Bmem cells. Flow cytometric detection of SARS-CoV-2-specific Bmem cells enables detection of long-term immune memory following infection or vaccination for COVID-19."

21 December 2020

Ann Intern Med: Comparison of Knowledge and Information-Seeking Behavior After General COVID-19 Public Health Messages and Messages Tailored for Black and Latinx Communities : A Randomized Controlled Trial

> "The paucity of public health messages that directly address communities of color might contribute to racial and ethnic disparities in knowledge and behavior related to coronavirus disease 2019 (COVID-19).
>
> To determine whether physician-delivered prevention messages affect knowledge and information-seeking behavior of Black and Latinx individuals and whether this differs according to the race/ethnicity of the physician and tailored content.
>
> Participants viewed 3 video messages regarding COVID-19 that varied by physician race/ethnicity, acknowledgement of racism/inequality, and community perceptions of mask-wearing.
>
> 7174 Black (61.3%) and 4520 Latinx (38.7%) participants were included in the analysis. The intervention reduced the knowledge gap incidence from 0.085 to 0.065 (incidence rate ratio, [IRR], 0.737 [95% CI, 0.600 to 0.874]) but did not significantly change information-seeking incidence. For Black participants, messages from race/ethnic-concordant physicians increased information-seeking incidence from 0.329 (for discordant physicians) to 0.357 (IRR, 1.085 [CI, 1.026 to 1.145]).
>
> Physician-delivered messages increased knowledge of COVID-19 symptoms and prevention methods for Black and Latinx respondents. The desire for additional information increased with race-concordant messages for Black but not Latinx respondents. Other tailoring of the content did not make a significant difference."

Emerg Infect Dis: Susceptibility of Domestic Swine to Experimental Infection with Severe Acute Respiratory Syndrome Coronavirus 2

> "Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the agent that causes coronavirus disease, has been shown to infect several species. The role of domestic livestock and associated risks for humans in close contact with food production animals remains unknown for many species. Determining the susceptibility of pigs to SARS-CoV-2 is critical to a One Health approach to manage potential risk for zoonotic transmission. We found that pigs are susceptible to SARS-CoV-2 after oronasal inoculation. Among 16 animals, we detected viral RNA in group oral fluids and in nasal wash from 2 pigs, but live virus was isolated from only 1 pig. Antibodies also were detected in only 2 animals at 11 and 13 days postinoculation but were detected in oral fluid samples at 6 days postinoculation, indicating antibody secretion. These data highlight the need for additional livestock

assessment to determine the potential role of domestic animals in the SARS-CoV-2 pandemic."

JAMA Intern Med: Excess Mortality in California During the Coronavirus Disease 2019 Pandemic, March to August 2020

"This time-series analysis examines the excess number of deaths across population subgroups in California during the COVID-19 pandemic."

Nature: Underdetection of COVID-19 cases in France threatens epidemic control

"As countries in Europe gradually relaxed lockdown restrictions after the first wave, test-trace-isolate strategies became critical to maintain COVID-19 viral activity at low levels. Reviewing their shortcomings can provide elements to consider in light of the second wave currently underway in Europe. Here we estimate the rate of detection of COVID-19 symptomatic cases in France after lockdown through the use of virological and participatory syndromic surveillance data coupled with mathematical transmission models calibrated to regional hospitalizations. Our findings indicate that around 90,000 incident symptomatic infections, corresponding to 9 out 10 cases, were not ascertained by the surveillance system in the first 7 weeks following lockdown from May 11 to June 28 2020, although the test positivity rate did not exceed WHO recommendations (5%). The median detection rate increased from 7% [6-8]% to 38% [35-44]% over time, with large regional variations, owing to a strengthening of the system as well as a decrease of epidemic activity. According to participatory surveillance data, only 31% of individuals with COVID-19-like symptoms consulted a doctor in the study period. This suggests that large numbers of symptomatic COVID-19 cases did not seek medical advice despite recommendations, as confirmed by serological studies. Encouraging awareness and same-day healthcare-seeking behavior in suspect cases is critical to improve detection. However, the capacity of the system remained insufficient even at the low levels of viral circulation achieved after lockdown, and was predicted to deteriorate rapidly with increasing epidemic activity. Substantially more aggressive, targeted, and efficient testing with easier access is required to act as a pandemic-fighting tool. Testing strategy will be once again of critical value to lift current restrictive measures in Europe and avoid a third wave."

20 December 2020

MMWR: The Advisory Committee on Immunization Practices' Interim Recommendation for Use of Moderna COVID-19 Vaccine — United States, December 2020

"On December 18, 2020, the Food and Drug Administration issued an Emergency Use Authorization (EUA) for the Moderna COVID-19 vaccine.

On December 19, 2020, after a transparent, evidence-based review of available data, the Advisory Committee on Immunization Practices (ACIP) issued an interim recommendation for use of the Moderna COVID-19 vaccine in persons aged ≥18 years for the prevention of COVID-19.

Use of all COVID-19 vaccines authorized under an EUA, including the Moderna COVID-19 vaccine, should be implemented in conjunction with ACIP's interim recommendations for allocating initial supplies of COVID-19 vaccines."

18 December 2020

BMC Med: Cardiovascular implications of COVID-19 versus influenza infection: a review

"Due to the overlapping clinical features of coronavirus disease 2019 (COVID-19) and influenza, parallels are often drawn between the two diseases. Patients with pre-existing cardiovascular diseases (CVD) are at a higher risk for severe manifestations of both illnesses. Considering the high transmission rate of COVID-19 and with the seasonal influenza approaching in late 2020, the dual epidemics of COVID-19 and influenza pose serious cardiovascular implications. This review highlights the similarities and differences between influenza and COVID-19 and the potential risks associated with coincident pandemics.

COVID-19 has a higher mortality compared to influenza with case fatality rate almost 15 times more than that of influenza. Additionally, a significantly increased risk of adverse outcomes has been noted in patients with CVD, with ~ 15 to 70% of COVID-19 related deaths having an underlying CVD. The critical care need have ranged from 5 to 79% of patients hospitalized due to COVID-19, a proportion substantially higher than with influenza. Similarly, the frequency of vascular thrombosis including deep venous thrombosis and pulmonary embolism is markedly higher in COVID-19 patients compared with influenza in which vascular complications are rarely seen. Unexpectedly, while peak influenza season is associated with increased cardiovascular hospitalizations, a decrease of ~ 50% in cardiovascular hospitalizations has been observed since the first diagnosed case of COVID-19, owing in part to deferred care.

In the coming months, increasing efforts towards evaluating new interventions will be vital to curb COVID-19, especially as peak influenza season approaches. Currently, not enough data exist regarding co-infection of COVID-19 with influenza or how it would progress clinically, though it may cause a significant burden on an already struggling health care system. Until an effective COVID-19 vaccination is available, high coverage of influenza vaccination should be of utmost priority."

17 December 2020

NEJM: REGN-COV2, a Neutralizing Antibody Cocktail, in Outpatients with Covid-19

> "In this ongoing, double-blind, phase 1–3 trial involving nonhospitalized patients with Covid-19, we investigated two fully human, neutralizing monoclonal antibodies against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein, used in a combined cocktail (REGN-COV2) to reduce the risk of the emergence of treatment-resistant mutant virus. Patients were randomly assigned (1:1:1) to receive placebo, 2.4 g of REGN-COV2, or 8.0 g of REGN-COV2 and were prospectively characterized at baseline for endogenous immune response against SARS-CoV-2 (serum antibody–positive or serum antibody–negative). Key end points included the time-weighted average change in viral load from baseline (day 1) through day 7 and the percentage of patients with at least one Covid-19–related medically attended visit through day 29. Safety was assessed in all patients.
>
> Data from 275 patients are reported. The least-squares mean difference (combined REGN-COV2 dose groups vs. placebo group) in the time-weighted average change in viral load from day 1 through day 7 was −0.56 log10 copies per milliliter (95% confidence interval [CI], −1.02 to −0.11) among patients who were serum antibody–negative at baseline and −0.41 log10 copies per milliliter (95% CI, −0.71 to −0.10) in the overall trial population. In the overall trial population, 6% of the patients in the placebo group and 3% of the patients in the combined REGN-COV2 dose groups reported at least one medically attended visit; among patients who were serum antibody–negative at baseline, the corresponding percentages were 15% and 6% (difference, −9 percentage points; 95% CI, −29 to 11). The percentages of patients with hypersensitivity reactions, infusion-related reactions, and other adverse events were similar in the combined REGN-COV2 dose groups and the placebo group.
>
> In this interim analysis, the REGN-COV2 antibody cocktail reduced viral load, with a greater effect in patients whose immune response had not yet been initiated or who had a high viral load at baseline. Safety outcomes were similar in the combined REGN-COV2 dose groups and the placebo group."

NEJM: Tocilizumab in Patients Hospitalized with Covid-19 Pneumonia

> "We randomly assigned (in a 2:1 ratio) patients hospitalized with Covid-19 pneumonia who were not receiving mechanical ventilation to receive standard care plus one or two doses of either tocilizumab (8 mg per kilogram of body weight intravenously) or placebo. Site selection was focused on the inclusion of sites enrolling high-risk and minority populations. The primary outcome was mechanical ventilation or death by day 28.
>
> A total of 389 patients underwent randomization, and the modified intention-to-treat population included 249 patients in the tocilizumab group and 128 patients in the placebo

group; 56.0% were Hispanic or Latino, 14.9% were Black, 12.7% were American Indian or Alaska Native, 12.7% were non-Hispanic White, and 3.7% were of other or unknown race or ethnic group. The cumulative percentage of patients who had received mechanical ventilation or who had died by day 28 was 12.0% (95% confidence interval [CI], 8.5 to 16.9) in the tocilizumab group and 19.3% (95% CI, 13.3 to 27.4) in the placebo group (hazard ratio for mechanical ventilation or death, 0.56; 95% CI, 0.33 to 0.97; P = 0.04 by the log-rank test). Clinical failure as assessed in a time-to-event analysis favored tocilizumab over placebo (hazard ratio, 0.55; 95% CI, 0.33 to 0.93). Death from any cause by day 28 occurred in 10.4% of the patients in the tocilizumab group and 8.6% of those in the placebo group (weighted difference, 2.0 percentage points; 95% CI, -5.2 to 7.8). In the safety population, serious adverse events occurred in 38 of 250 patients (15.2%) in the tocilizumab group and 25 of 127 patients (19.7%) in the placebo group.

In hospitalized patients with Covid-19 pneumonia who were not receiving mechanical ventilation, tocilizumab reduced the likelihood of progression to the composite outcome of mechanical ventilation or death, but it did not improve survival. No new safety signals were identified."

ICYMI (older than the last 2 weeks)

Pediatr Infect Dis J: COVID-19 and Multisystem Inflammatory Syndrome in Latin American Children: A Multinational Study (published online 16 October 2020)

"To date, there are no comprehensive data on pediatric COVID-19 from Latin America. This study aims to assess COVID-19 and Multisystem Inflammatory Syndrome (MIS-C) in Latin American children, to appropriately plan and allocate resources to face the pandemic on a local and international level.

Ambispective multicenter cohort study from 5 Latin American countries. Children 18 years of age or younger with microbiologically confirmed SARS-CoV-2 infection or fulfilling MIS-C definition were included.

Four hundred nine children were included, with a median age of 3.0 years (interquartile range 0.6–9.0). Of these, 95 (23.2%) were diagnosed with MIS-C. One hundred ninety-one (46.7%) children were admitted to hospital and 52 (12.7%) required admission to a pediatric intensive care unit. Ninety-two (22.5%) patients required oxygen support: 8 (2%) were started on continuous positive airway pressure and 29 (7%) on mechanical ventilation. Thirty-five (8.5%) patients required inotropic support. The following factors were associated with pediatric intensive care unit admission: preexisting medical condition (P < 0.0001), immunodeficiency (P = 0.01), lower respiratory tract infection (P < 0.0001), gastrointestinal

symptoms (P = 0.006), radiologic changes suggestive of pneumonia and acute respiratory distress syndrome (P < 0.0001) and low socioeconomic conditions (P = 0.009).

This study shows a generally more severe form of COVID-19 and a high number of MIS-C in Latin American children, compared with studies from China, Europe and North America, and support current evidence of a more severe disease in Latin/Hispanic children or in people of lower socioeconomic level. The findings highlight an urgent need for more data on COVID-19 in Latin America."

PLoS Biol: A network medicine approach to investigation and population-based validation of disease manifestations and drug repurposing for COVID-19 (09 November 2020)

"The global coronavirus disease 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has led to unprecedented social and economic consequences. The risk of morbidity and mortality due to COVID-19 increases dramatically in the presence of coexisting medical conditions, while the underlying mechanisms remain unclear. Furthermore, there are no approved therapies for COVID-19. This study aims to identify SARS-CoV-2 pathogenesis, disease manifestations, and COVID-19 therapies using network medicine methodologies along with clinical and multi-omics observations. We incorporate SARS-CoV-2 virus–host protein–protein interactions, transcriptomics, and proteomics into the human interactome. Network proximity measurement revealed underlying pathogenesis for broad COVID-19-associated disease manifestations. Analyses of single-cell RNA sequencing data show that co-expression of ACE2 and TMPRSS2 is elevated in absorptive enterocytes from the inflamed ileal tissues of Crohn disease patients compared to uninflamed tissues, revealing shared pathobiology between COVID-19 and inflammatory bowel disease. Integrative analyses of metabolomics and transcriptomics (bulk and single-cell) data from asthma patients indicate that COVID-19 shares an intermediate inflammatory molecular profile with asthma (including IRAK3 and ADRB2). To prioritize potential treatments, we combined network-based prediction and a propensity score (PS) matching observational study of 26,779 individuals from a COVID-19 registry. We identified that melatonin usage (odds ratio [OR] = 0.72, 95% CI 0.56–0.91) is significantly associated with a 28% reduced likelihood of a positive laboratory test result for SARS-CoV-2 confirmed by reverse transcription–polymerase chain reaction assay. Using a PS matching user active comparator design, we determined that melatonin usage was associated with a reduced likelihood of SARS-CoV-2 positive test result compared to use of angiotensin II receptor blockers (OR = 0.70, 95% CI 0.54–0.92) or angiotensin-converting enzyme inhibitors (OR = 0.69, 95% CI 0.52–0.90). Importantly, melatonin usage (OR = 0.48, 95% CI 0.31–0.75) is associated with a 52% reduced likelihood of a positive laboratory test result for SARS-CoV-2 in African Americans after adjusting for age, sex, race, smoking history, and various disease comorbidities using PS matching. In summary, this study presents an integrative network medicine platform for predicting disease manifestations

associated with COVID-19 and identifying melatonin for potential prevention and treatment of COVID-19."

Selected Literature: Preprints

Preprints are found on preprint servers such as arXiv, bioRxiv, and medRxiv; they are commonly used for biomedical research. Preprints may later be published in peer-reviewed journals. Per medRxiv: "Preprints are preliminary reports of work that have not been certified by peer review. They should not be relied on to guide clinical practice or health-related behavior and should not be reported in news media as established information."

bioRxiv: Rapid inactivation in vitro of SARS-CoV-2 in saliva by black tea and green tea (posted 28 December 2020)

> "Saliva plays major roles in human-to-human transmission of the SARS-CoV-2. Recently we reported that black, green and oolong tea significantly inactivated SARS-CoV-2 within 1 min. Theaflavin-3,3'-di-gallate (TFDG), theasinensin A (TSA) and (-) epigallocatechin gallate (EGCG) were involved in the anti-viral activities. Here we examined how long period is required for the compounds to inactivate the virus. We also assessed whether tea inactivates SARS-CoV-2 diluted in human saliva. Treatment of SARS-CoV-2 with 500 µM TFDG or TSA for 10 sec reduced the virus titer to undetectable levels (less than 1/1,000). Black and green tea decreased virus titer to less than 1/100 within 10 sec even in saliva. These findings suggest a possibility that intake of, or gargling with, tea may inactivate SARS-CoV-2 in saliva in infected individuals, which may eventually attenuate spread of COVID-19 within a population, although clinical studies are required to test this hypothesis by determining the intensity and duration of the anti-viral effect of tea in saliva in humans."

medRxiv: Characterizing Long COVID in an International Cohort: 7 Months of Symptoms and Their Impact (posted 27 December 2020)

> "Objective To characterize the symptom profile and time course in patients with Long COVID, along with the impact on daily life, work, and return to baseline health.
>
> Design International web-based survey of suspected and confirmed COVID-19 cases with illness lasting over 28 days and onset prior to June 2020.
>
> Setting Survey distribution via online COVID-19 support groups and social media
>
> Participants 3,762 respondents from 56 countries completed the survey. 1166 (33.7%) were 40-49 years old, 937 (27.1%) were 50-59 years old, and 905 (26.1%) were 30-39 years old. 2961 (78.9%) were women, 718 (19.1%) were men, and 63 (1.7%) were nonbinary. 8.4%

reported being hospitalized. 27% reported receiving a laboratory-confirmed diagnosis of COVID-19. 96% reported symptoms beyond 90 days.

Results Prevalence of 205 symptoms in 10 organ systems was estimated in this cohort, with 66 symptoms traced over seven months. Respondents experienced symptoms in an average of 9.08 (95% confidence interval 9.04 to 9.13) organ systems. The most frequent symptoms reported after month 6 were: fatigue (77.7%, 74.9% to 80.3%), post-exertional malaise (72.2%, 69.3% to 75.0%), and cognitive dysfunction (55.4%, 52.4% to 58.8%). These three symptoms were also the three most commonly reported overall. In those who recovered in less than 90 days, the average number of symptoms peaked at week 2 (11.4, 9.4 to 13.6), and in those who did not recover in 90 days, the average number of symptoms peaked at month 2 (17.2, 16.5 to 17.8). Respondents with symptoms over 6 months experienced an average of 13.8 (12.7 to 14.9) symptoms in month 7. 85.9% (84.8% to 87.0%) experienced relapses, with exercise, physical or mental activity, and stress as the main triggers. 86.7% (85.6% to 92.5%) of unrecovered respondents were experiencing fatigue at the time of survey, compared to 44.7% (38.5% to 50.5%) of recovered respondents. 45.2% (42.9% to 47.2%) reported requiring a reduced work schedule compared to pre-illness and 22.3% (20.5% to 24.3%) were not working at the time of survey due to their health conditions.

Conclusions Patients with Long COVID report prolonged multisystem involvement and significant disability. Most had not returned to previous levels of work by 6 months. Many patients are not recovered by 7 months, and continue to experience significant symptom burden."

medRxiv: Estimated transmissibility and severity of novel SARS-CoV-2 Variant of Concern 202012/01 in England (posted 26 December 2020)

"A novel SARS-CoV-2 variant, VOC 202012/01, emerged in southeast England in November 2020 and appears to be rapidly spreading towards fixation. We fitted a two-strain mathematical model of SARS-CoV-2 transmission to observed COVID-19 hospital admissions, hospital and ICU bed occupancy, and deaths; SARS-CoV-2 PCR prevalence and seroprevalence; and the relative frequency of VOC 202012/01 in the three most heavily affected NHS England regions (South East, East of England, and London). We estimate that VOC 202012/01 is 56% more transmissible (95% credible interval across three regions 50-74%) than preexisting variants of SARS-CoV-2. We were unable to find clear evidence that VOC 202012/01 results in greater or lesser severity of disease than preexisting variants. Nevertheless, the increase in transmissibility is likely to lead to a large increase in incidence, with COVID-19 hospitalisations and deaths projected to reach higher levels in 2021 than were observed in 2020, even if regional tiered restrictions implemented before 19 December are maintained. Our estimates suggest that control measures of a similar stringency to the national lockdown implemented in England in November 2020 are unlikely to reduce the effective reproduction number Rt to less than 1, unless primary schools,

secondary schools, and universities are also closed. We project that large resurgences of the virus are likely to occur following easing of control measures. It may be necessary to greatly accelerate vaccine roll-out to have an appreciable impact in suppressing the resulting disease burden."

Events and Presentations

WHAT: CDC COCA: COVID-19 Vaccines: Update on Allergic Reactions, Contraindications, and Precautions

WHEN: Wednesday, 30 December 2020 1400-1500 ET

DETAILS: "During this COCA call, clinicians will give an overview of recommendations for use of COVID-19 vaccines in certain populations. Clinicians will learn more about the recent reports of anaphylaxis following vaccination, as well as CDC's updated clinical considerations around contraindications and precautions to vaccination.

If you are unable to attend the live COCA Call, the recording will be available for viewing on the COCA Call webpage a few hours after the live event ends."

See: https://emergency.cdc.gov/coca/calls/2020/callinfo_123020.asp

News in Brief

A New Variant

There is a great deal of uncertainty surrounding the new SARS-CoV-2 variant ("B.1.1.7.") (CIDRAP; see also the CDC brief), which has 17 mutations (Science; see also preliminary virology report).

Many countries are instituting additional travel restrictions or bans for anyone coming from the UK (Reuters).

Even with restrictions, multiple countries (including Canada with 2 cases in Ontario) report cases with the new variant (CIDRAP).

Researchers looking at the new UK strain think it is already in the US, and likely arrived in mid-November (CNN).

The first case of the UK variant in the US was confirmed on Tuesday, 29 December; the case is in a Colorado man in his 20s with no history of travel (WaPo).

Vaccines

After authorizing the Pfizer COVID-19 vaccine, the EU has started its vaccine rollout (NPR).

Novavax has started enrollment of the phase 3 trial of NVX-CoV2373, its coronavirus vaccine; of note this vaccine can be stored and distributed at above-freezing temperatures (35°-- 46°F) (NIH).

The Stanford vaccine algorithm debacle -- in which many frontline healthcare workers were excluded from COVID-19 vaccine priority -- demonstrates bias at multiple levels (STAT).

"The lightning-fast quest for COVID vaccines — and what it means for other diseases" (Nature).

Treatment and Therapies

"Rural hospitals are overwhelmed by the coronavirus, causing patients to be flown hundreds of miles from their homes to get care" (BuzzFeed News).

Numerous national organizations, including the National Academy of Medicine, have called for action to implement crisis standards of care during COVID-19 surges (NAM).

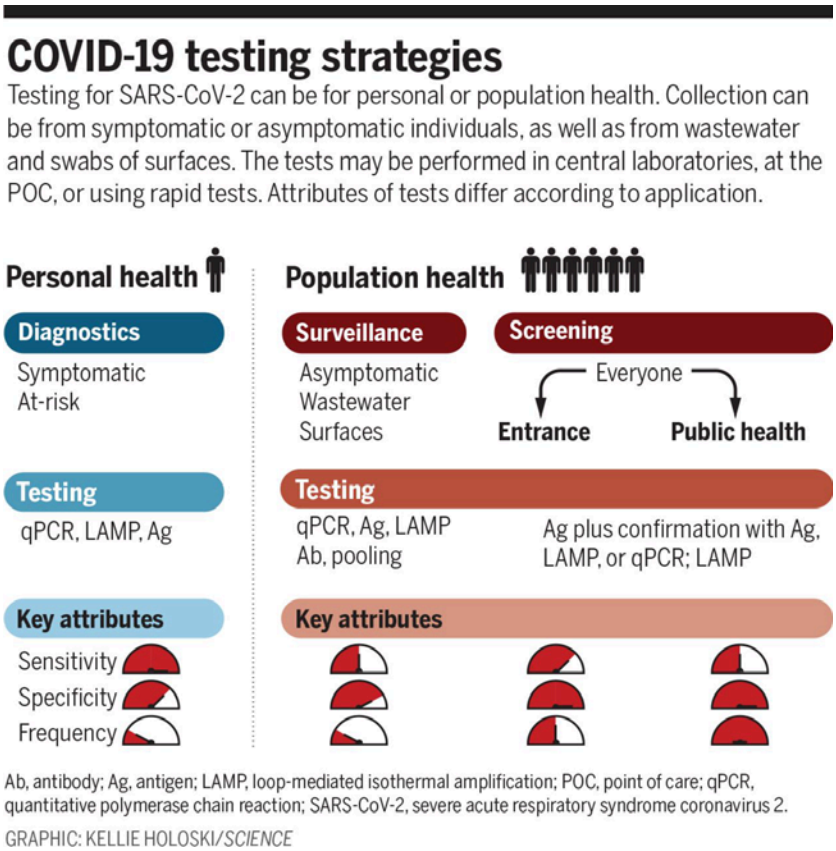
Exposure, Testing, and Risks

"COVID-19 testing: One size does not fit all" (Science). --->

With confirmation of positive COVID-19 tests in personnel at a research station in Antarctica, SARS-CoV-2 has now impacted all continents (NPR).

Families are using obituaries to warn of the risks of COVID-19 (LAT).

The NIH is funding 8 studies to look at risk factors for COVID-19--related multisystem inflammatory syndrome in children (NIH).



Thanks, Coronavirus

"Drive-by burials and FaceTime farewells: Grief in the Covid era will weigh on the American psyche for years to come" (STAT).

"The coronavirus can cause insomnia and long-term changes in our nervous systems. But sleep could also be a key to ending the pandemic" (Atlantic).

"Ways to look after yourself and others in 2021" (Nature).

Long Reads

"The year we lost" (Atlantic).

"Where year two of the pandemic will take us" (Atlantic).

Other Outbreaks and Threats

The FDA has approved Ebanga, a human monoclonal antibody, to treat Ebola infection in adults and children (FDA).

Elk in Wyoming have tested positive for chronic wasting disease (CIDRAP); a whitetail deer found on Blackfeet Nation land in Montana tested positive earlier this month (BFWD).

A new study suggests the Reston ebolavirus spreads in pigs as a severe respiratory illness, raising concerns it could spread to humans (NIH).

Finally, 2020 Will Be In Our Hindsight

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2020: A Pandemic Timeline

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